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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,296	03/13/2001	Vladimir Efimov	AM-00102.P.1-US	2109

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10/08/2004

Biotechnology Law Group
658 Mansoian Avenue
Solana Beach, CA 92075

EXAMINER

MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 10/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/805,296

Applicant(s)

EFIMOV ET AL.

Examiner

Thomas McKenzie, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 97-129 is/are pending in the application.
- 4a) Of the above claim(s) 97-107 and 114-129 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 108-113 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 March 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 and 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to amendments filed on 7/26/04. Applicant has amended claims 108 and 110. Claims 108-113 were previously rejected. No claims were designated as containing allowable subject matter. There are thirty-three claims pending and six under consideration. Claims 108-113 are compound claims. This is the third action on the merits. The application concerns some nucleobase compounds linked to a 4-hydroxyproline and uses thereof.

Response to Amendment

2. Applicants' amendment to claim 108, changing a carbonyl group to phosphorus containing an oxygen anion corrects a typo and changes the formula back to that of the amendment of 3/13/01. This formula has support in structure XII on page 54 with the addition of the end-capping radicals G and E required by the laws of chemical valence. Thus, there is no new matter.

3. The deletion of "a reporter group" from the definition of radicals B¹ and B² renders moot the objection concerning the trademarks Cy3 and Cy5 discussed in point #6 of the previous office action. These trademarked dyes were part of the definition of "reporter group". The indefinites rejection made in point #12 is also rendered moot. Applicants deletion of the relevant terms overcomes the indefiniteness rejections made in points #9-#12 of the previous action.

Election/Restrictions

4. This application contains claims 97-107 and 114-129 drawn to an invention nonelected with traverse in Paper No. 14. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

5. Objection remains to claims 108-113 as containing non-elected subject matter. The claimed compounds, compositions, and methods that employ them present a variable core. Formula of claim 108 contains compounds drawn to the non-elected inventions to the extent it reads on compounds other than B^2 = a purine or a pyrimidine.

Applicants make no remarks concerning this objection.

Specification

6. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486

F.2d 577, 179 USPQ 167 (CCPA 1973). The issue concerning the PCT applications and the meaning of "non-naturally occurring nucleobase" is discussed below.

Applicants make no remarks concerning this objection.

Abstract

7. Applicant is still reminded of the proper content of an abstract of the disclosure. A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." The abstract is too generic. Examiner suggests claim 108, including the figure.

Applicants make no remarks concerning this objection.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 108-113 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The elected subject matter of claim 108

includes radical B¹ selected from "a non-naturally occurring nucleobase". This phrase is indefinite because it is unclear what are the structures of the claimed radicals.

Applicants define "non-naturally occurring nucleobase" in lines 5-17, page 14 of the specification. The definition uses open language "such as" and "can be". Applicants list a number of bases not found in natural nucleosides in lines 9-14, page 14. What bases in addition to these are being claimed? The passage cited incorporates by reference two US Patents and four PCT applications. While US Patents may be incorporated by reference, PCT applications may not. Search of the two US Patents, reveals no usage of the phrase "non-naturally occurring nucleobase". In lines 18-23, column 5 of US Patent 6,150,510 there is a definition of "unnatural bases". The definition also uses open language "such as, for example". All of the specific radical listed in the passage cited appear to be incorporated into Applicants' list. What additional radicals are being incorporated from US Patent 6,150,510?

Applicants point to lines 18-26, page 13 of the specification and argue that the term "nucleobase" is both defined in the specification and art-recognized as to its meaning. This is not persuasive. The passage on page 13 describes nucleic acid analogues but is silent as to the meaning of "a non-naturally occurring nucleobase".

Is a nucleobase the same thing as a nucleic acid monomer or is it something else? Are the analogues of these monomers "non-natural" or not? The word "nucleobase" has been found definite in these claims. Other than the fact that "a non-naturally occurring nucleobase" is presumably different than a nucleobase, this does nothing to clarify the structures of these radicals.

The Examiner suggests using the bases listed in lines 9-14, page 14 to specify what is intended here or citing a textbook in biochemistry or a review article to illustrate the art-recognized meaning of this term as discussed in the recent telephone interview of 3/22/04.

9. Claims 110 and 111 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrases "a phosphono peptide nucleic acid monomer" is indefinite. Again, nowhere in the specification is this term defined *verbatim*. What is the structure of this radical? In lines 24-27, page 2 Applicants introduce the abbreviation "pPNAs" for phosphono peptide nucleic acid. In lines 16-19, page 12, Applicants define "a phosphono peptide nucleic acid" but fail to specify if this is a monomer. They use open language "comprising" "such as". In lines 23-26, page 13, Applicants define "monomer unit of a peptide nucleic acid" but fail to specify if this is a phosphorus containing

peptide. The definition includes "nucleobase (or nucleobase analogue, nucleobase-binding unit, ligand, intercalator, reporter group or label)". The indefiniteness of these terms has been discussed in the previous office action. The nucleobase "is covalently attached to an amino acid or amino acid derivative or analog". Does amino acid refer to the twenty naturally occurring amino acids, which are coded for in DNA, or are all compounds containing any acid and amine group intended? The issue of derivative or analogue was discussed previously. The three structures **II-IV**, pages 20, 22, and 24 are described as hydroxyproline and aryl phosphono peptide nucleic acid monomers. Is this what is meant? The Examiner understands that hydroxyproline is an amino acid, which may be incorporated into a peptide, but hydroxyproline itself is not a peptide. An aryl group is not a peptide but structure IV apparently may contain additional peptides in radicals G and E. The Examiner suggests using structures **II-IV**, if that is what is intended.

Applicants point to the passages spanning line 1, page 20 to line 15, page 25 and line 1, page 40 to line 19, page 45 as indicating what they intend. The former passage defines "a hydroxyproline-1 phosphono peptide nucleic acid monomer or "Hyp-1NA" monomer", "a hydroxyproline-2 phosphono peptide nucleic acid monomer or "Hyp-2NA" monomer", and "an aryl phosphono peptide nucleic acid monomer or "pPNA-Ar-1" monomer". None of these three defines *ipso verba* the

meaning of "a phosphono peptide nucleic acid monomer". Are these monomer units the same or something different? Is "a phosphono peptide nucleic acid monomer" just a portion of the three monomers recited above? If so what part? Neither of the first two structures even contains a proline residue, which is a carboxylic acid. Removal of a pyrrolidine ring from the first residue leaves $C(R^{16})(R^{17}) P(O)(O^-)E$. Is this "a phosphono peptide nucleic acid monomer"? Removal of a pyrrolidine ring from the second residue leaves $P(O)(O^-)E$. This differs from the structures I-IV and differs from the $C(R^{16})(R^{17}) P(O)(O^-)E$ residue just discussed. Removal of the aryl radical from the third structure leaves $N(-A-B) C(R^{16})(R^{17}) P(O)(O^-)E$. This just gets more confusing.

The latter passage cited by Applicants, in fact, defines three different groups, "a phosphono peptide nucleic acid-hydroxyproline peptide nucleic acid dimer or "pPNA-HypNA" dimer", "a serine peptide nucleic acid-phosphono peptide nucleic acid dimer or "SerNA-pPNA" dimer", and "a phosphono peptide nucleic acid-serine peptide nucleic acid dimer or "pPNA-SerNA" dimer." These three dimers certainly contain the phrase " phosphono peptide nucleic acid" but do not *ipso verba* define what is meant by "a phosphono peptide nucleic acid monomer". The structures themselves are internally inconsistent. For example, when the Examiner mentally removes what appears to be a serine residue from "a serine peptide

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nucleic acid-phosphono peptide nucleic acid dimer" what remains is a lengthy residue containing A^2-B^2 attached to a nitrogen atom. When the Examiner mentally removes what appears to be serine from "a phosphono peptide nucleic acid-serine peptide nucleic acid dimer" what remains is a residue containing A^1-B^1 to a nitrogen atom. Which residue represents the structure of "a phosphono peptide nucleic acid monomer"? Are both structures being claimed? Are there others? These three radical differ from the three radical defined on pages 20-25. Is everything to be included?

In the telephone interview, Applicants proposed incorporating the formulas of their desired phosphono peptide radical into the structures but have failed do do so.

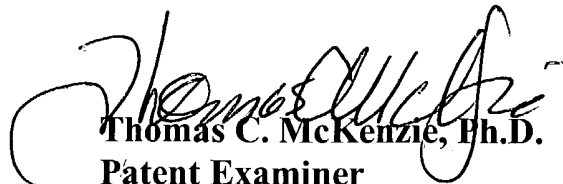
Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date

of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

12. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact Mukund Shah SPE of 1624 at (571)-272-0674.


Thomas C. McKenzie, Ph.D.
Patent Examiner
Art Unit 1624